

### REMARKS/ARGUMENTS

Reconsideration of the Examiner's rejection of the present application is requested respectfully in view of the following remarks. In accordance with Rule 1.116, the amendments to the claims are to comply with requirements of form or to present the claims in better form for consideration on appeal.

### STATUS OF THE CLAIMS

At the time of the present Action, claims 1 to 6, and 23 to 25 were pending in this patent application. Claims 1 to 6, and 23 to 25 have been amended. No claims have been canceled or added. Therefore, claims 1 to 6, and 23 to 25 are presented for consideration.

### SUMMARY OF OFFICE ACTION

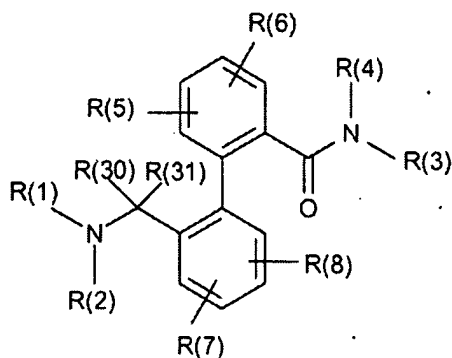
Claims 1 to 6, and claims 23 to 25, stand rejected under 35 U.S.C. §112, first paragraph, for lack of enablement.

### THE REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1 to 6, and claims 23 to 25 stand rejected under 35 U.S.C. §112, first paragraph, for lack of sufficient disclosure to enable one skilled in the art to make and use all of the claimed compounds. Applicants submit that all compounds encompassed by the presently amended claims are fully enabled by the specification.

In response to the issues raised by the Examiner in the Action, applicants have amended the claims to align more closely to the examples presented in the specification. For the benefit of the Examiner, following is a presentation of claim 1, as amended, with references to relevant examples inserted in brackets.

1. (Currently amended) A compound of the formula I,



in which:

R(1) is C(O)OR(9) or C(O)NR(12)R(13);

R(9) is  $C_xH_{2x}-R(14)$ ;

x is 0, 1, 2, 3 or 4,

where x cannot be 0 if R(14) is OR(15);

R(14) is OR(15) or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br,  $CF_3$ , COOMe [Example 2h], alkyl having 1, 2, 3 or 4 carbon atoms [Example 14a], and alkoxy having 1, 2 or 3 carbon atoms [Examples 2m, 11a];

R(15) is phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br and  $CF_3$ ;

R(12) is defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or  $CF_3$ ;

R(3) is  $C_yH_{2y}-R(16)$ ;

y is 0, 1, 2, 3 or 4,

where y cannot be 0 if R(16) is OR(17) or  $SO_2Me$ ;

R(16) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms,  $CF_3$ ,  $C_2F_5$ ,  $C_3F_7$ ,  $CH_2F$ ,  $CHF_2$ , OR(17),  $SO_2Me$ , phenyl or naphthyl,

where phenyl and naphthyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I and  $CF_3$ ;

R(17) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms,  $CF_3$  or phenyl,

where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I and  $CF_3$ ;

or

R(3) is CHR(18)R(19);

- R(18) is hydrogen or  $C_zH_{2z}$ -R(16), where R(16) is defined as indicated above;  
     z is 0, 1, 2 or 3;  
 R(19) is COOH, CONH<sub>2</sub>, CONR(20)R(21), COOR(22) or CH<sub>2</sub>OH;  
 R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms,  $C_vH_{2v}$ -CF<sub>3</sub>  
     or  $C_wH_{2w}$ -phenyl,  
     where phenyl is unsubstituted;  
     v is 0, 1, 2 or 3;  
     w is 0, 1, 2 or 3;  
 R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;  
 R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms;  
 R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or CF<sub>3</sub>;  
 R(5), R(6), R(7) and R(8)  
     independently of one another are hydrogen, F, Cl, Br, I, CF<sub>3</sub> or OH [Example 16b]; and  
 R(30) and R(31)  
     independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms;  
 or a pharmaceutically acceptable salt thereof.

The Examiner has raised the issue that the examples in the specification do not include sufficient enablement support for the possible substituents in the claims. The examples in the specification include numerous compounds with halogen and CF<sub>3</sub> substituted phenyl groups. In addition, in the above version of claim 1, applicants refer to specific examples and the substituents they support. Example 2h (page 44) shows a phenyl group with a COOMe substituent. Example 14a (page 85) includes an alkyl substituted phenyl group. Examples 2m (page 46) and 11a (page 74) show alkoxy substituted phenyl groups. Example 16b (page 87) includes an OH substituent on the core biphenyl moiety. The measured IC<sub>50</sub> values for these examples as well as numerous other examples are all listed in the table on pages 96-97.

Applicant wishes to refer the Examiner to Reaction Scheme 4 as set forth on page 26 of the application. The synthetic route depicted in this reaction scheme, which includes a Suzuki coupling reaction, was developed for combinatorial synthesis of compounds encompassed by the present claims of this application. This scheme is suitable for the synthesis of claimed compounds with all of the stated options for R5-R8, as well as all of the possible phenyl substituents. If the starting materials (substituted phenyl compounds only) are not commercially available, their preparation, based in particular on methods for introducing the residues R5 and R6, and R7 and R8 onto phenyl rings, would have been well known to one skilled in the art at the priority date of the present application. That is, the two substituted phenyl compound starting

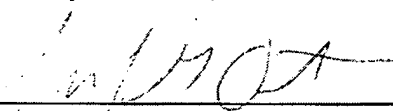
materials which would be combined by the coupling reaction depicted in Scheme 4 are each relatively simple compounds which could be obtained commercially or readily synthesized.

In view of the specific examples noted above, and in view of the discussion of Reaction Scheme 4 above, it is submitted that the present specification is fully enabling for the synthesis of all of the residue values for the R5-R8 substituents, and the phenyl substituents for R14 and R15. The test data reported in the table at pages 96-97 provides ample support to enable one skilled in the art to use the presently claimed compounds. Therefore, it is submitted that the specification fully enables one skilled in the art to make and use all of the claimed compounds. Reconsideration and withdrawal of the present rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

It is submitted that all of the claims pending in the present application are now in condition for allowance, and action to that effect is respectfully requested.

The Commissioner is hereby authorized to charge any additional fees or credit any overpayment resulting from this Amendment to Deposit Account 18-1982.

Respectfully submitted,



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Ronald G. Ort, Reg. No. 26,969  
Attorney for Applicant

sanofi-aventis U.S. LLC.  
Patent Department  
Route #202-206 / P.O. Box 6800  
Bridgewater, NJ 08807-0800  
Telephone (908) 231-2551  
Telefax (908) 231-2626